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The Opioid Litigation: The FDA is MIA

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ABSTRACT

It is readily agreed that federal preemption of state tort law alters the balance between federal and state power. Federal preemption is a high-profile defense in almost all modern products liability cases. It is thus surprising to see how little attention has been given to federal preemption by courts and commentators in the opioid litigation. Opioid litigation provides a lens through which I explore the role of state and federal courts and the Food and Drug Administration (FDA) in striking the right balance of power. My purpose here is not to resolve the divide among the few courts that have weighed in on the preemption defense in the opioid cases before them; instead, it is to highlight the appropriate inquiry in which the courts should engage. Namely courts should scrutinize the regulatory actions taken by the FDA and evaluate the extent to which state tort law actions fall within or outside of the bounds of the risk analysis already undertaken by the FDA. Such an analysis would put pressure on the FDA to weigh in—either on its own or as invited by the courts—on the balance between its regulatory actions and the need for state tort law causes of action. The courts would then scrutinize input from the agency under "hard look" review. No longer could the FDA remain on the sidelines, as it has to date, amidst a public health crisis that is now playing out in the courts.

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INTRODUCTION

In 2017, the U.S. Department of Health and Human Services declared the opioid epidemic a public health emergency.[1] In that same year, what had hitherto been a trickle of government lawsuits against opioid drug manufacturers, distributors, and retailers became a flood, as more than one hundred states, counties, and cities filed claims. In December 2017, the U.S. Judicial Panel on Multidistrict Litigation ("MDL") transferred more than one hundred government claims against opioid drug manufacturers, distributors, sellers, and prescribers to the U.S. District Court for the Northern District of Ohio.[2] State attorneys general filed additional suits in state courts.

The lawsuits allege various state law causes of action, including that the drug manufacturers improperly marketed or over-promoted opioids for long-term use to treat chronic pain; that they minimized the risks of addiction; that they encouraged excessive prescribing that created a larger supply for potential diversion; and that they created a "public nuisance" by taking these actions.[3] Whether litigation is an appropriate response to the opioid epi-

1. Press Release, U.S. Dep't. of Health & Hum. Servs., HHS Acting Secretary Declares Public Health Emergency to Address National Opioid Crisis (Oct. 26, 2017), https://bit.ly/2yj7n0g [https://perma.cc/9YPH-Q5JZ].

2. *In re* Nat'l Prescription Opiate Litig., 290 F. Supp. 3d 1375, 1380 (J.P.M.L. 2017).

3. *See In re* Nat'l Prescription Opiate Litig., No. MDL 2804, 2018 WL 4895856, at *34 (N.D. Ohio Oct. 5, 2018) (Magistrate's report and recommendation).

demic has been forcibly debated;[4] less attention has been given to the propriety of the specific state law causes of action involved—namely over-promotion, risk of diversion, or public nuisance.

Curiously, the role of the federal Food and Drug Administration (FDA) has not been front and center—in either the public debate or, more surprisingly, in the high-profile litigation. In this Article, I highlight the significance of the FDA's regulatory process for the approval and labeling of opioids—specifically for long-term use against chronic pain—and the role this process plays in opioid litigation. The defense of federal preemption of state tort law claims for FDA-approved drugs (and medical devices) is featured prominently in products liability litigation against drug (and medical device) manufacturers—but it has gained little traction in the opioid cases in state and federal courts. Those eager to see drug manufacturers, distributors, and sellers held responsible and accountable might applaud this state of affairs. But, as I will argue in this Article, the courts' lack of engagement with the federal preemption defense comes at a cost—namely a missed opportunity for the courts (and thereby the public) to interrogate the regulatory role and accountability of the FDA.

My purpose here is not to resolve the divide in the few courts that have weighed in on the preemption defense in the opioid cases before them. Instead, the goal of this Article is to highlight the appropriate inquiry in which the courts should engage. I argue that courts should scrutinize the regulatory actions taken by the FDA and evaluate the extent to which state tort law actions fall within or outside of the bounds of the risk analysis already undertaken by the FDA. This analysis would put pressure on the FDA to weigh in on the balance between its regulatory actions and the need for state tort law causes of action. Courts, scrutinizing input from the FDA under "hard look" review, could ensure that the agency does not remain on the sidelines, and that it acknowledges the role it has and will continue to play in the opioid epidemic.

I. OPIOID REGULATION: THE FDA'S ACTIVE ROLE

The FDA has been actively involved in the regulation of opioids. As Lars Noah reminds us, "[f]ederal agencies represent the first . . . line of defense against the misuse of pain management

4. *See, e.g.*, Abbe R. Gluck, et al., *Civil Litigation and the Opioid Epidemic: The Role of Courts in a National Health Crisis*, 46 J. OF L., MED. & ETHICS 351 (2018); Derek Carr, Corey S. Davis & Lainie Rutkow, *Reducing Harm Through Litigation Against Opioid Manufacturers? Lessons from The Tobacco Wars*, 133 PUB. HEALTH REP. 207 (2018).

technologies."[5] Opioids are pharmaceutical drugs that must be approved by the FDA as safe and effective and are available only by prescription. The pre-market new drug approval ("NDA") process for brand-name Class III drugs is a rigorous and lengthy safety review process, predicated on the drug manufacturer submitting three phases of clinical trial evidence.[6] The FDA faces the classic trade-off between Type I errors (false positive)—approving drugs that turn out not to be safe and effective—and Type II errors (false negative)—withholding approval from drugs that are in fact safe and effective. The FDA has a reputation for being risk averse and tending towards minimizing Type I errors, by maintaining very stringent *ex ante* review criteria. In the contexts of opioids, the FDA must navigate this choice, balancing the potential societal harms of dangerous drugs such as opioids against the needs of patients in chronic pain.

The FDA approved the opioid drug OxyContin in 1995.[7] Oxycontin uses a time-release formula designed to offer sustained relief over a 12-hour period to patients with chronic moderate-to-severe pain.[8] Manufacturers Purdue Pharma and Abbott Labs promoted their drug as presenting a lower risk of abuse and diversion, given that the time-release version would not provide a quick euphoric effect upon initial ingestion. But the companies failed to anticipate that drug abusers, to defeat the slow-release feature, could chew, crush, dissolve, or scrape the coating off the tablets, thus leaving stronger doses of oxycodone than those found in individual Percocet or Percodan tablets. They could then ingest, snort, or inject the substance. Reports indicate that hundreds (if not thousands) of people have died after overdosing in this fashion, typically as a result of acute pulmonary edema.[9]

In addition to approving high-risk drugs as safe and effective, the FDA also carefully controls the information and warnings provided by the manufacturer during the FDA's labeling pre-approval process. Moreover, the FDA conducts post-market oversight. In

5. Lars Noah, *Challenges in the Federal Regulation of Pain Management Technologies*, 31 J.L. MED. & ETHICS 55, 64 (2003).

6. *FDA's Drug Review Process: Continued*, U.S. FOOD & DRUG ADMIN., https://bit.ly/2w3qN8N [https://perma.cc/5KVW-XKAJ].

7. *Timeline of Selected FDA Activities and Significant Events Addressing Opioid Misuse and Abuse*, U.S. FOOD & DRUG ADMIN., https://bit.ly/2xGQBrv [https://perma.cc/87XG-WT7T].

8. "In contrast, the older drug products in this class (including the related hydrocodone drugs such as Vicodin and Lortab) may offer uneven relief over just a 3[–]4[-]hour period." Noah, *supra* note 5, at 62.

9. *Id.* at 62.

July 2001, the FDA mandated labeling revisions for OxyContin to provide stronger warnings. A few months later, the FDA convened one of its advisory committees to provide additional recommendations.[10]

In what follows, I canvas the significant regulatory actions taken by the FDA in the post-market surveillance period. It is worth emphasizing at the outset that this account does not represent the full regulatory record but is instead gleaned from the bits and pieces of the FDA administrative record that surfaced in opioid litigations, including in parties' briefs to the courts and courts' motions, orders, and decisions.

A. FDA Denial of Citizen Petitions Requesting Labeling Changes

FDA regulations provide stakeholders with the opportunity to file a "citizen petition" to request the agency to "take or refrain from taking"[11] an administrative action, such as labeling changes to FDA-approved drugs.

In January 2004, the Connecticut Attorney General submitted a citizen petition requesting a labeling change for OxyContin. The petition claimed that OxyContin was not a true 12-hour drug and that its use on a more frequent dosing schedule increased its risk for diversion and abuse. In September 2008, the FDA denied the petition, concluding the evidence failed to support that using OxyContin more frequently than every 12 hours posed greater risks.[12]

In July 2012, a coalition of concerned doctors, Physicians for Responsible Opioid Prescribing ("PROP"), filed a citizen petition requesting the FDA to alter its indicated uses for opioids. PROP stated that clinicians were under the false impression that chronic opioid therapy was an evidence-based treatment for chronic noncancer pain and asked the FDA to prohibit manufacturers from marketing opioids for conditions for which the use of opioids had not been proven safe and effective.[13]

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10. *Id.* at 63.

11. Initiation of administrative proceedings, 21 C.F.R. § 10.25 (1989); Citizen petition, 21 C.F.R. § 10.30 (2016).

12. Letter from Janet Woodcock, MD., Dir., Ctr. for Drug Eval. and Research, U.S. Food & Drug Admin., to Richard Blumenthal, Conn. Attorney Gen. (Sept. 9, 2008), https://bit.ly/35ahG30 [https://perma.cc/RK9S-DR9Y] [hereinafter 2008 Woodcock Letter].

13. *See* Letter from Physicians for Responsible Opioid Prescribing to the U.S. Food and Drug Admin. (July 25, 2012) (on file with the American Society of Anesthesiologists); Letter from Janet Woodcock, MD., Dir., Ctr. for Drug Eval. and Research, U.S. Food and Drug Admin., to Andrew Kolodny, President, Physicians

In 2013, the FDA responded to the petition, granting it in part and rejecting it in part. Recognizing the grave risks associated with opioid use, the FDA required opioid manufacturers to include in their drug labels a warning that opioids should be used only when alternative treatments were inadequate. The FDA declined to recommend a daily maximum dose or the maximum duration of opioid treatment and stated that more controlled studies were needed concerning the long-term use of opioids. The agency acknowledged that high rates of addiction were concerning and ordered opioid manufacturers to conduct post-approval studies on the long-term use of the medications.[14]

B. FDA Approval of Specific Requirements for Extended-Release Opioids

On July 9, 2012, the FDA approved a Risk Evaluation and Mitigation Strategy ("REMS") for extended release, long-action opioids.[15] The REMS directs physicians to "[u]nderstand and appropriately use screening tools for addiction or abuse to help assess potential risks associated with chronic opioid therapy and to help manage patients using ER/LA [extended release and long-acting] opioid analgesics."[16] The REMS contains requirements for distribution of a Medication Guide with each prescription filled, as well as a requirement that training be made available to all those who prescribe ER/LA opioids. It further specifies the necessary elements of prescriber training in the "FDA Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics" ("FDA Blueprint"). The FDA Blueprint provides prescribers with guidance to enable appropriate ER/LA opioid prescribing practices and information to use when counseling patients about the risks and benefits of ER/LA opioid use.[17]

C. FDA Informal Communications

In May 2019, a medical officer in the FDA Division of Anesthesia, Analgesia, and Addiction Products wrote a letter entitled "Opioids Regulatory Background for the June 11–12, 2018,

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for Responsible Opioid Prescribing (Sept. 10, 2013) https://bit.ly/3bP2MkS [https://perma.cc/RK2J-HTAH] [hereinafter 2013 Woodcock Letter].

14. *See* 2013 Woodcock Letter, *supra* note 13, at 11–12.

15. U.S. FOOD & DRUG ADMIN., EXTENDED-RELEASE (ER) AND LONG-ACTING (LA) OPIOID ANALGESICS RISK EVALUATION AND MITIGATION STRATEGY (REMS) (2012), http://bit.ly/2UwjlLG [https://perma.cc/797J-AF4G].

16. *Id.* at 3.

17. *See* 2013 Woodcock Letter, *supra* note 13, at 4.

DSaRM [Drug Safety and Risk Management Advisory Committee]/AADPAC [Anesthetic and Analgesic Drug Products Advisory Committee] Meeting."[18] This letter was not part of official correspondence by the FDA, but it was cited by defendants to support the proposition that the FDA disagreed with labeling changes that plaintiffs claim were necessary.[19]

Beyond discussing some of the background health effects associated with opioid use, the defendants argued that the letter reinforced the FDA's position against setting maximum daily doses for prescription opioids—a major issue in the 2012 PROP citizen petition. The FDA noted that "no particular dose of any opioid has been determined to be a cutoff point between safe-for-use or unsafe-for-use."[20] In support, the letter cited the findings of the Pain Management Best Practices Inter-Agency Task Force, created as a part of the Comprehensive Addiction and Recovery Act of 2016, which declined to recommend "any absolute limits on the individual dose or total daily dose of opioid analgesics."[21]

Moreover, the FDA letter also casts sharp doubt on what it termed "well-meaning attempts to address the opioid crisis without adequate scientific evidence to support such actions."[22] In particular, the letter pointed to the inappropriate use of a 2016 Center for Disease Control (CDC) Guideline for Prescribing Opioids for Chronic Pain to support the idea that opioids should be subject to a maximum daily dose. The misinterpretation and misapplication of these guidelines, the letter maintained, "contribut[ed] to substantial harms to patients, particularly patients with chronic pain, who were forced to taper their previously stable opioid doses to lower doses, or who were forced to discontinue their opioids through forced tapers or patient abandonment."[23] These harms include suicidal ideation, suicidal self-directed violence, severe withdrawal accompanied by worsening pain and profound loss of function, and the increased

18. U.S. FOOD & DRUG ADMIN., MEMORANDUM FROM NING HU, MED. OFFICER, CTR. FOR DRUG EVALUATION AND RESEARCH (May 13, 2019), https://bit.ly/3eWme1C [https://perma.cc/6HE3-ECAA] [hereinafter HU MEMO].

19. Manufacturer Defendants' Motion for Summary Judgment that Plaintiffs' State-Law Claims are Preempted and Their Federal Claims are Precluded at 13, *In re* Nat'l Prescription Opiate Litig., No. 1:17 MD 2804 (N.D. Ohio July 19, 2019).

20. HU MEMO, *supra* note 18, at 10.

21. *Id.* at 12.

22. *Id.* at 10.

23. *Id.* at 11. The letter further noted that the extent of the misuse of the 2016 CDC Guidance was substantial enough to cause the agency to release a statement in 2019 titled "*CDC Advises Against Misapplication of the [2016] Guideline for Prescribing Opioids for Chronic Pain*." *Id.*

chance patients may seek relief from dangerous and illicit sources of opioids.[24]

In contrast to maximum daily doses or other rigid guidelines, the letter emphasized the Inter-Agency Task Force's conclusion that "emphasis should be placed on the importance of individualized care, the use of multimodal approaches to acute pain management, and the use of multidisciplinary approaches to chronic pain management," consistent with the facets of the FDA Blueprint that focused on patient/provider counseling.[25] Interestingly, the letter suggested it was "the over reliance on the use of prescription opioid analgesics," and the associated societal harms that have led to intense scrutiny of opioids, rather than defective labeling or design.[26] Indeed, nowhere did the letter make any reference to controversy over changes to opioid labeling practices beyond a tame observation that "[t]he product labeling contains a summary of the essential scientific information needed for the safe and effective use of the drug."[27]

II. OPIOID LITIGATION: SPOTLIGHT ON THE FDA

Federal preemption is a high-profile defense in almost all modern products liability cases. It is thus surprising to see how little attention has been given to federal preemption by courts and commentators in the opioid litigation. The relative inattention cannot be explained by a lack of vigor for federal preemption on the part of defendant manufacturers. Indeed, as explored in Section A, defendants have consistently raised the preemption defense in each of the litigated cases. Moreover, the few courts that have wrestled with the preemption defense have found it to be a difficult, close issue.

But there remains substantive uncertainty regarding the appropriate inquiry or factors that should guide courts' preemption determinations. As I shall argue, a significant lacuna is input from the FDA. This is so both in terms of providing the full regulatory record documenting the agency's decades-long back-and-forth with opioid drug manufacturers, as well as clarifying the agency's position on whether the state law claims would upend its regulatory directives and aims. Thus far, no court has called for the views of the FDA, nor has the FDA intervened on its own accord. In Section B, I apply the "agency reference model" for preemption and attempt

24. *Id.* at 10.
25. *Id.* at 12.
26. *Id.* at 10.
27. *Id.* at 13.

to map out the significant questions that must be addressed by courts.

A. In Search of the Federal Preemption Defense

The U.S. Supreme Court has set forth different standards that govern federal preemption of state law claims against brand-name drug manufacturers and of those claims brought against generic drug manufacturers. State law failure-to-warn claims against brand-name manufacturers are only preempted where the manufacturer provides "clear evidence" that the FDA would have rejected the proposed labeling changes.[28] State law failure-to-warn and design defect claims against generic drug manufacturers are preempted, in light of the fact that generic (unlike brand-name) drug manufacturers cannot unilaterally change their labels; instead, they must abide by federal "sameness" directives, requiring their labels and warnings to match those of their brand-name equivalents.[29]

Numerous courts have concluded that state law claims involving an FDA-approved prescription brand-name drug are preempted when a plaintiff alleges one of two scenarios: (1) a defendant unlawfully included misleading information or (2) a defendant failed to include important warnings on the drug's label, where the defendant could unilaterally alter the label and/or there is "clear evidence" the FDA would not approve a change to the label if sought by the defendant.[30] Preemption determinations in claims against generic manufacturers are even more likely in light of the "sameness" directives that bar any action to alter the drug's label that differs from action already taken by brand-name equivalents. Federal preemption challenges persist in drug litigation with parties' attempts to push the boundaries of the framework set forth by the U.S. Supreme Court.

1. Opioid Manufacturers' Vigorous Preemption Arguments

Defendants in opioid litigation have moved to dismiss (or for summary judgment on) plaintiffs' state law misrepresentation claims on the basis of federal preemption.[31] The thrust of the pre-

28. Wyeth v. Levine, 555 U.S. 555, 571 (2009).

29. PLIVA, Inc. v. Mensing, 564 U.S. 604, 624 (2011).

30. *See, e.g.*, Dolin v. GlaxoSmithKline LLC, 901 F.3d 803, 812 (7th Cir. 2018); Cerveny v. Aventis, Inc., 855 F.3d 1091, 1099 (10th Cir. 2017).

31. Memorandum of Law in Support of the Manufacturer Defendants' Joint Motion to Dismiss Plaintiffs' Second Amended Complaint, *In re* Nat'l Prescription Opiate Litig., No. 1:17 MD 2804 (N.D. Ohio May 25, 2018) [hereinafter Motion to Dismiss]; Manufacturer Defendants' Motion for Summary Judgment that Plaintiffs' State-Law Claims are Preempted and Their Federal Claims are Precluded, *In*

emption argument is that the FDA's various decisions regarding the risks and medically appropriate uses of opioids conflict with the allegations raised in the state law claims.[32] Put another way, state law claims are preempted where they would require the opioid manufacturer to make statements about the safety or efficacy of the drug in its marketing materials that differ from those required by the FDA.

Defendants' arguments are twofold: First, state claims are preempted because they seek to impose liability for lawful promotion of an FDA-approved product for an FDA-approved use. Second, state law claims are preempted because the FDA has previously declined to alter the labeling and/or warnings.

Starting with the first set of arguments, opioid defendants claim that their marketing and promotion of opioid medications is entirely consistent with the FDA's approval of their respective drug, including its indication for chronic pain, as well as duration of use and daily dosage.[33] For example, the FDA approved long-term use of a twice daily dose of Purdue's OxyContin to treat chronic pain. More controversially, the defendants also justify their use and promotion of the concept of "pseudoaddiction"—a drug-seeking behavior that mimics addiction from patients receiving inadequate pain relief—on the ground the FDA-approved labeling likewise embodied this concept.[34] Opioid defendants also assert doctors are able to use addiction risk-screening tools to identify and safely prescribe opioids to patients, even those predisposed to addiction, by pointing to the FDA-mandated REMS that requires drug manufacturers to provide risk-benefit information to physicians.[35] And finally, they tout the effectiveness of abuse-deterrent opioid

re Nat'l Prescription Opiate Litig., No. 1:17 MD 2804 (N.D. Ohio July 28, 2019) [hereinafter Motion for Summary Judgment].

32. *See* Motion to Dismiss, *supra* note 31, at 34; Motion for Summary Judgment, *supra* note 31, at 4.

33. State v. Purdue Pharma Inc., No. 217-2017-CV-00402, 2018 WL 4566129, at *2–4 (N.H. Super. Ct. Sept. 18, 2018) (arguing, on its own behalf, that Purdue is entitled to dismissal because "each of the . . . alleged misrepresentations the State has identified involves statements or conduct that are consistent with the FDA-approved labeling for its medications or with other regulatory decisions of the FDA"); Grewal v. Purdue Pharma L.P., No. ESX-C-245-17, 2018 WL 4829660, at *5–7 (N.J. Super. Ct. Ch. Div. Oct. 02, 2018) (arguing likewise).

34. *See, e.g.*, Defendants Purdue Pharma L.P., Purdue Pharma Inc., and the Purdue Frederick Company Inc.'s Motion to Dismiss for Failure to State a Claim and Memorandum of Law in Support at 11, State *ex rel.* Hunter v. Purdue Pharma L.P., No. CJ-2017-816 (Okla. Dist. Ct. Sept. 22, 2017) [hereinafter OK Motion to Dismiss].

35. North Dakota v. Purdue Pharma, LP, et al., No. 08-2018-CV-01300, slip op. at 12 (N.D. Dist. Ct. May 10, 2019) (granting motion to dismiss).

formulations to prevent abuse and addiction, consistent with the FDA-approved labeling that indicates that the ingredients are intended to make the tablet more difficult to misuse and abuse.[36]

But a manufacturer of an FDA-approved brand-name drug cannot wield federal preemption to immunize itself against state law failure-to-warn claims solely on the basis that the FDA approved the drug and its accompanying labeling. Rather, as the U.S. Supreme Court made clear in *Wyeth v. Levine*,[37] the manufacturer remains responsible for its labeling (which includes all marketing materials) at all times.[38] Moreover, should new risk evidence come to light, the manufacturer is empowered by federal regulation to add information or warnings to its FDA-approved label while simultaneously informing the FDA.[39] In other words, the manufacturer cannot claim immunity from state law claims on the basis that it could not add to the information in the FDA-approved label without seeking prior FDA approval. Only where the manufacturer provides "clear evidence" that the FDA would not have approved the additional information or warnings is the state law failure-to-warn claim preempted.[40] And in *Merck Sharpe & Dohme, Inc. v. Albrecht*,[41] the Court clarified that the "clear evidence" standard was one for the court (not jury) to decide.[42] The Court also elaborated on the substance of the "clear evidence" standard, stating that "in a case like *Wyeth*," impossibility preemption requires the "manufacturer to show that it fully informed the FDA of the justifications for the warning required by state law and that the FDA, in turn, informed the drug manufacturer that the FDA would not approve changing the drug's label to include that warning."[43]

Accordingly, the opioid defendants advance the second set of arguments, maintaining that they have met the *Wyeth* "clear evidence" standard. They point first and foremost to the FDA's rejection of the 2012 PROP citizen petition, which among other things

36. *Id.* at 13.

37. Wyeth v. Levine, 555 U.S. 555 (2009).

38. *Id.* at 570–71 (2009); *see also id.* at 608 (Alito, J. dissenting) (citing 21 C.F.R § 314.80; 21 U.S.C. § 355(k)).

39. *Id.* at 568 (describing the "changes being affected" regulation, which allows the manufacturer to change the label to "add or strengthen a contraindication, warning, precaution, or adverse reaction" or to "add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product" upon filing a supplemental application with the FDA) (citing 21 C.F.R. §§ 314.70(c)(6)(iii)(A), (C)).

40. *Id.* at 571.

41. Merck Sharpe & Dohme, Inc. v. Albrecht, 139 S. Ct. 1668 (2019).

42. *Id.* at 1672.

43. *Id.* at 1678.

sought to limit the use of opioids in non-cancer patients to 90 days, as "clear evidence" the FDA would have rejected labeling changes concerning the long-term use of opioids, the concept of pseudoaddiction, and addiction withdrawal.[44] In its response to the PROP petition, the FDA concluded that the available information did not demonstrate a causal relationship between dosage and adverse events.[45] Moreover, as the defendants argue, the "FDA did so based on its comprehensive review of the available scientific information on the benefits and risks of ER/LA opioids and with its express acknowledgment of the limitations in the available data on long-term use."[46]

Finally, the defendants note that the FDA mandated further studies to provide an empirical foundation for any labeling revisions to provide different or additional information regarding risks and benefits to physicians: "As to certain risks that were already included in the labeling for the medications, FDA required manufacturers of ER/LA opioids to conduct additional studies and further assess those risks along with the benefits of use, and those studies are underway."[47] But, according to the defendants, "[u]ntil such evidence is available or [the] FDA requires labeling changes, state law claims that would force [opioid manufacturers] to make statements that are inconsistent with the labeling [the] FDA has required would conflict directly with its federal law obligations."[48]

2. A Puzzle in the Courts: Avoidance and Partial Responses

Federal preemption is typically front and center in modern products liability litigation, especially concerning pharmaceuticals and medical devices. The relative inattention given to federal preemption in the opioid litigation is thus, at least at first glance, puzzling.

In the Oklahoma litigation brought by the Attorney General against Purdue, for example, the state court's final decision did not mention preemption at all.[49] In a prior order, the court summarily

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44. *In re* Opioid Litig., No. 400000/2017, 2018 WL 3115102, at *9 (N.Y. Sup. Ct. June 18, 2018). In addition, the FDA rejected the 2004 petition from the Attorney General of Connecticut, which claimed that OxyContin was not a twelve-hour drug and should be dosed more frequently. *See* 2008 Woodcock Letter, *supra* note 12, at 1.

45. *See* 2013 Woodcock Letter, *supra* note 13, at 16–17.

46. OK Motion to Dismiss, *supra* note 34, at 6.

47. *Id.* at 9.

48. *Id.*

49. *See generally* State *ex rel.* Hunter v. Purdue Pharma L.P., No. CJ-2017-816, 2019 WL 4019929 (Okla. Dist. Ct. Aug. 26, 2019).

rejected preemption without any explanation: "After review of the briefs and oral arguments from the parties, the [c]ourt finds and orders that the State's Petition sufficiently states its claims[,] and those claims should not be dismissed based on preemption or pursuant to the Primary Jurisdiction doctrine or the Court's inherent power."[50] In a similar fashion, a Delaware state court dispensed with the manufacturers' preemption arguments with a single line: "The State's allegations of labeling inconsistent with FDA approvals ('pseudoaddiction,' softening and minimization) are sufficient to survive dismissal on the grounds of federal preemption."[51]

One explanation is that plaintiffs have strategically framed their causes of action so as to avoid federal preemption, and courts have narrowly construed the domain of federal preemption to apply to failure-to-warn (and design defect) product liability claims. In other words, where courts have addressed the federal preemption defense, the brevity of their discussion is a function of their finding that the bulk of claims fall outside the scope of the preemption defense. One such category of claims is fraud. Thus, as an Ohio state court explained, "[T]he allegations of the Plaintiff's complaint primarily sound in fraud and not the propriety of the labeling of opioids. . . . [D]rug labeling does not preclude fraud claims. The claims set forth in Plaintiff's complaint are not barred by the FDA's approval of labeling or the doctrine of preemption as to Defendants' branded or unbranded labeling."[52]

A second, related, category of cases implicates aggressive off-label promotion amounting to misrepresentations by the drug manufacturer. For example, the State of New Hampshire brought an action in state court alleging that "'Purdue aggressively marketed its opioids for long-term use to treat chronic pain through misrepresentations that were intended to lead doctors to prescribe the drugs even in circumstances where they were inappropriate, *i.e.*, to disregard cautions that the FDA itself has recognized as appropriate and necessary.'"[53] In other words, according to the State, "'Purdue

50. State *ex rel.* Hunter v. Purdue Pharma. L.P., No. CJ-2017-816, 2017 WL 10152334, at *1 (Okla. Dist. Ct. Dec. 6, 2017) (order denying motion to dismiss).

51. State *ex rel.* Jennings v. Purdue Pharma L.P., No. N18C-01-223 MMJ CCLD, 2019 WL 446382, at *4 (Del. Super. Ct. Feb. 4, 2019).

52. State *ex rel.* DeWine v. Purdue Pharma L.P., No. 17 CI 261, 2018 WL 4080052, at *3 (Ohio Ct. Com. Pl. Aug. 22, 2018). As the court further explained: "The parties agree that the FDA approved the labeling for opioids for long-term treatment. However, it is evident in the Plaintiff's complaint that its claims are based upon misrepresentations made by the Defendants concerning the use and safety of opioids which go far beyond the labeling." *Id.*

53. State v. Purdue Pharma Inc., No. 217-2017-CV-00402, 2018 WL 4566129, at *3 (N.H. Super. Ct. Sep. 18, 2018) (citation omitted).

marketed opioids in a manner that *is contrary to, inconsistent with, or outside of* their FDA-approved labels.'"[54] Such allegations, the court reasoned, "'do[ ] not seek a change to the FDA-approved labeling of Purdue's drugs.'"[55] The court concluded that Purdue failed to show that the state's allegations wholly reflect *conduct* that was consistent with the FDA-approved labeling and thus rejected Purdue's preemption defense.[56]

Along similar lines, courts have been persuaded that preemption defenses do not pertain to causes of action that focus on the drug manufacturer's *business practices* as distinct from labeling choices. For example, in the New York state case, the plaintiffs alleged that the manufacturer defendants made presentations to medical professionals and others about the efficacies of long-term use of opioids as though those statements were supported by substantial evidence. Further, plaintiffs contended "that the manufacturer defendants knew about the addictive effects of opioids . . . but minimized those effects when promoting, marketing, and advertising the drugs."[57] The New York state court held that these allegations, which "are not based upon the same theories and scientific evidence presented in the PROP petition," instead concern the defendants' business practices and were therefore not preempted.[58]

In a similar vein, the Ohio federal Multidistrict Litigation (MDL) court declined to read the plaintiffs' allegations as "premised upon inappropriate labeling or a fraud on the FDA" and instead interpreted the state law claims as "fraudulent marketing in

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54. *Id.*

55. *Id.* The court concluded that Purdue's statements that

> OxyContin's abuse-deterrent properties "*prevent* tampering," result in a drug that "*cannot* be crushed or snorted," and in practice "*prevent or reduce* opioid abuse" may reasonably be read as attributing more significance to the abuse-deterrent properties than the FDA intended when it seemingly found the abuse-deterrent properties merely make the drug somewhat "more difficult to manipulate."

Id. at *4.

56. *Id.*

57. *In re* Opioid Litig., No. 400000/2017, 2018 WL 3115102, at *9 (N.Y. Sup. Ct. June 18, 2018).

> For example, the plaintiffs allege[d] that the manufacturer defendants used the concept of pseudoaddiction as an excuse to encourage medical professionals to prescribe more or higher doses of opioids despite knowledge of the high risk of abuse. The manufacturer defendants allegedly distributed treatment guidelines to professionals, which indicated that a clinician's *first* response to treating pseudoaddiction was to increase dosing although other adequate treatment options were available.

Id.

58. *Id.*

the promotion and sale of their opioids."[59] The court moreover held that a state law duty to monitor the sale of opioids with due care was not inherently "inconsistent with the purposes of the FDCA[ ] and thus not preempted."[60]

Interestingly, courts have followed this line of reasoning even in the context of generic drug preemption, notwithstanding the fact that U.S. Supreme Court jurisprudence strongly favors preemption of claims against generic manufacturers. For example, a Rhode Island state court sharply distinguished prior U.S. Supreme Court cases involving "claims of products liability, including failure-to-warn and design defect" from the "common-law claims such as negligence and public nuisance" before it.[61] Echoing some of its sister state jurisdictions that refused to preempt off-label promotion claims against brand-name manufacturers, the court held that "[w]hile [generic] pharmaceutical manufacturers are required to comply with FDA regulations with respect to labeling, they are under no obligation to engage in off-label promotion."[62] Thus, the court rejected the argument that the State's claims against a generic drug manufacturer based on misleading or fraudulent marketing were preempted.[63]

The Ohio federal MDL court similarly extended its reasoning from the brand-name drug context to generic drugs. In addressing generic manufacturers' preemption arguments, the court

> agreed only with the *narrow* argument that liability could not be "impose[d] upon the Generic Manufacturers . . . for not sending warnings that the Brand-Name Manufacturers had not sent," . . .

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59. *In re* Nat'l Prescription Opiate Litig., No. 1:17 MD 2804, 2019 WL 4178591, *2 (N.D. Ohio Sept. 3, 2019) (order denying defendants' motion for summary judgment). This order by Judge Polster responded to four separate summary judgment motions by various groupings of defendants (Non-RICO Small Distributors, Pharmacies and Distributors, Manufacturers, and Generic Manufacturers). *Id.* at *1. The order summarized the findings and conclusions of three separate magistrate Report and Recommendations and issued a final order regarding preemption, holding that the state law claims are not preempted and denying summary judgment. *Id.* at *12.

60. *Id.* at *2 (internal citation omitted). The court also observed that "plaintiffs were not seeking to enforce the provisions of the Federal Food, Drug, and Cosmetic Act ('FDCA'), but their allegations were 'of the type that would traditionally be brought as state law claims [prior to the enactment of the FDCA].'" *Id.* (internal citation omitted). Otherwise, their claims would be preempted. *See Buckman Co. v. Plaintiffs' Legal Committee,* 531 U.S. 341, 353 (2001).

61. State v. Purdue Pharma L.P., No. PC-2018-4555, 2019 R.I. Super. LEXIS 95, at *60 (Super. Ct. Aug. 16, 2019).

62. *Id.*

63. *Id.* at *61.

> "because it would be impossible for Generic Manufacturers to comply with both federal law and the supposed state law duty."[64]

However, the court continued, to the extent that the state law claims are based on other theories—like "aggressive and misleading marketing and inadequate anti-diversion activities"—they were not preempted.[65]

Not all courts, however, make such a sharp distinction between preempted products liability claims and non-preempted marketing and off-label promotion claims. For example, in *State ex rel. Stenehjem v. Purdue Pharma L.P.*,[66] the state of North Dakota strategically avoided raising an inadequate warning theory; instead it raised claims for violations of state consumer fraud law, unconscionable business practices, and statutory public nuisance. Even though the State studiously avoided raising an inadequate labeling theory, the court nonetheless observed that the State did argue that Purdue could have and should have strengthened its labeling and warnings to include additional risks without prior FDA approval.[67] The court concluded that the allegedly improper marketing practices were consistent with FDA's product label; thus the claims were preempted under conventional drug preemption analysis.[68]

Finally, after *Wyeth* and *Albrecht*, the courts face lingering doctrinal uncertainty regarding what constitutes "clear evidence" the FDA would not have approved a particular warning or new information to a brand-name drug label. Some courts have accepted the argument that a response to a citizen petition can constitute such evidence. For example, having subjected the State's claims to preemption analysis, the North Dakota state court held that there was sufficiently "clear evidence" the FDA would not have changed the label on the basis of the agency's rejection of the PROP citizen peti-

64. *In re* Nat'l Prescription Opiate Litig., 2019 WL 4178591, at *6 (N.D. Ohio Sept. 3, 2019).

65. *Id.* at *6 (internal quotation marks omitted) (quoting *In re* Nat'l Prescription Opiate Litig., No. 1:17 MD 2804, 2019 WL 2468267, at *22 (N.D. Ohio, Apr. 1, 2019), *report and recommendation adopted in part, rejected in part*, No. 1:17 MD 02804, 2019 WL 3737023 (N.D. Ohio, June 13, 2019)). Moreover, with respect to the generic manufacturers' invocation of *Buckman* implied preemption, the court held that the generic manufacturers' argument "fails for the same reasons Manufacturers' preemption argument fails—namely, Plaintiffs' state law claims are not predicated upon violations of the FDA or CSA, nor are they accurately characterized as 'fraud on the FDA' or 'fraud on the DEA' claims." *Id.*

66. State *ex rel.* Stenehjem v. Purdue Pharma L.P., No. 08-2018-CV-01300, 2019 WL 2245743 (N.D. Dist. Ct. May 10, 2019).

67. *Id.* at *5.

68. *Id.* at *7–8.

tion.[69] As such, Purdue did not have a sufficient basis under *Wyeth*'s "clear evidence" standard to change the label. The court also relied on the REMS program "blueprint" to support the proposition that the FDA label incorporated the concept of pseudoaddiction.[70]

In contrast, the Ohio federal MDL court was "unable to conclude the PROP letter satisfied *Wyeth*'s clear-evidence standard [because] . . . the [c]ourt could not rule on the preemptive effect of the FDA letter in the absence of a full record."[71] The MDL court explicitly refused to follow the North Dakota decision, which it characterized as, "by leaps and bounds, an outlier on the question of preemption."[72] And, in a similar vein, the New York state court refused to credit the "less-than-definitive determination" concerning PROP's request for maximum dosage and treatment duration as meeting the *Wyeth* clear evidence threshold.[73] The court highlighted the fact that, in its response to PROP, and in light of the concerning high rates of addiction, the FDA requested "further exploration" of the long-term use of opioids, even though at that time

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69. Specifically, the court observed that

> [i]n 2013, the FDA addressed the same issues raised by the State[ ] and concluded that no modification to the product labeling was necessary. In response to a 2012 citizen's petition from PROP, the FDA studied the available scientific evidence and concluded that it supports the use of ER/LA opioids to treat chronic non-cancer pain.

Id. at *5 (citations omitted). The court then analyzed the various allegations made by the State and how they conflicted with statements the FDA has approved and concluded that the FDA has communicated its disagreement with the State's specific contention that Purdue "falsely and misleadingly touted the benefits of long-term opioid use and falsely and misleadingly suggested that these benefits were supported by scientific evidence." *Id.* (citation and internal quotation marks omitted); *accord* Cerveny v. Aventis, Inc., 855 F.3d 1091, 1105 (10th Cir. 2017).

70. State *ex rel.* Stenehjem, No. 08-2018-CV-01300, 2019 WL 2245743, at *6.

71. *In re* Nat'l Prescription Opiate Litig., No. 1:17 MD 2804, 2019 WL 4178591, at *3 (N.D. Ohio Sept. 3, 2019). As mentioned above, moreover, the court raised an alternative ground to reject preemption: "[E]ven if the Court were to agree with the argument the FDA letter had some preemptive effect, this would not preempt every theory of liability articulated by Plaintiffs, *e.g.*, fraudulent marketing and the failure to monitor and prevent opioid diversion." *Id.*

72. *Id.* at *5. Bolstering its conclusion, the court reasoned that,

> [f]irst, Plaintiffs simply have not proposed any label changes. Second, there is no evidence the FDA approved or endorsed Manufacturers' campaign message that the risk of addiction is manageable for patients with a history of addiction problems, or that signs of opioid addiction are actually pseudoaddiction ameliorated with *more* opioids.

Id.

73. *In re* Opioid Litig., No. 400000/2017, 2018 WL 3115102, at *11 (N.Y. Sup. Ct. June 18, 2018).

the petitioners did not present sufficient evidence to support their specific recommendations.[74]

B. Agency Reference Model: A Necessary Dialogue between Courts and the FDA

Courts struggle with articulating a coherent and consistent framework for analyzing preemption questions—and this is no doubt true in the context of the opioid litigation discussed above. In prior work, I have advanced an "agency reference model" for preemption decision-making, whereby courts would look to input from the relevant federal regulator in order to evaluate whether the state tort law clashes or impedes upon federal regulatory risk decisions.[75] The model is premised on the idea that tort and regulation work in tandem, and courts' preemption decisions provide an opportunity for an independent judicial check on regulators' choices and views in striking the optimal balance. Astutely aware of the potential for ideologically driven decisions on the part of regulators—as well as danger of political flip-flop in successive administrations—the model purposely calls for courts to "reference" input from federal regulating agencies, not accord "deference" to them. Applying "hard look" review, courts should scrutinize the basis for the agency's determination to ensure that there is sound empirical basis for its underlying decisions regarding incompatibility of competing state tort standards.[76]

The U.S. Supreme Court's *Wyeth* decision implicitly embraced such an "agency reference model." In that case, the Court tackled the issue of whether a manufacturer of an FDA-approved drug could nonetheless be held liable in tort for failure-to-warn. The manufacturer relied on a statement of the FDA, given in a preamble to a regulation governing the content of drug labels, which indicated that the agency's approval of labeling should preempt conflicting or contrary state law.[77] However, this was a sudden

74. *Id.*

75. *See generally* Catherine M. Sharkey, *Products Liability Preemption: An Institutional Approach*, 76 GEO. WASH. L. REV. 449 (2008).

76. *See* Catherine M. Sharkey, *Federalism Accountability: "Agency-Forcing" Measures*, 58 DUKE L.J. 2125, 2178–91 (2009) (elaborating upon this framework by looking to how heightened judicial review of preemptive regulations would operate in practice); Catherine M. Sharkey, *State Farm "With Teeth": Heightened Judicial Review in the Absence of Executive Oversight*, 89 N.Y.U. L. REV. 1589, 1634–46 (2014) (endorsing a system by which agencies' conflict preemption determinations would be subject to more demanding judicial scrutiny).

77. Wyeth v. Levine, 555 U.S. 555, 575 (2009) (citing Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. 3922 (Jan. 24, 2006)).

change (following a change in political administration) from the FDA's long-held position to the contrary.[78] The about-face in the preamble to the regulation—inserted after conclusion of the notice-and-comment process in which affected entities and interested persons could submit comments and attempt to challenge the findings of the agency—amounted to a "procedural flaw" in the administrative process.[79] The U.S. Supreme Court (unlike the state courts below) did take the administrative record before it seriously—with citations by the majority and dissent from the nearly 50-year administrative back-and-forth between the drug manufacturer and the FDA; moreover, the Court also considered the FDA's views on preemption.[80] However, instead of deferring thereto, the Court applied a form of "hard look" review to the FDA preamble, which, in light of the procedural flaw, did not withstand scrutiny. The majority also noted the fact that the FDA had changed its position, and its new stance did not emerge out of the appropriate administrative law notice-and-comment process.[81]

The *Abrecht* Court elaborated on *Wyeth* (particularly the "clear evidence" standard).[82] But questions still persist—many of which have implications for the agency reference model.

1. Key Unresolved Questions

One unresolved issue in the wake of *Albrecht* is which types of agency action trigger preemption. A second, related, issue is what is the required mechanism for this dialogue with the FDA, and how direct must the communication be? For example, does the FDA's rejection of a citizen petition suffice? Courts are thus far divided on this particular issue. Prior to *Albrecht*, the Tenth Circuit Court of Appeals held that the rejection of a citizen petition may constitute "clear evidence" that the FDA would have rejected a manufacturer-initiated change to a drug label.[83] But the New York opioids court resisted this line of cases, highlighting the fact that manufacturers have "superior access to information about their drugs, especially in the post[-]marketing phase as new risks emerge[.]"[84] As a result, the court could not conclude as a matter of law that the agency would have rejected manufacturers' change of label propos-

78. *Id.* at 578–79, 578 n.10.
79. *See id.* at 577.
80. *See id.* at 577–79, 578 nn.10–12.
81. *Id.* at 580.
82. Merck Sharpe & Dohme, Inc. v. Albrecht, 139 S. Ct. 1668, 1678 (2019).
83. *See* Cerveny v. Aventis, Inc., 855 F.3d 1091, 1105 (10th Cir. 2017).
84. *In re* Opioid Litig., No. 400000/2017, 2018 WL 3115102, at *9 (N.Y. Sup. Ct. June 18, 2018).

als meant to strengthen dosing instruction and administration of the drugs.[85]

2. Spotlight on Input from the FDA

Given the need for input from the FDA to fuel the agency reference model, courts will likely want a fairly comprehensive regulatory record at their disposal. This raises a particular issue. Will litigants be incentivized to provide such a record (as opposed to the status quo whereby litigants tend to supply bits and pieces that serve their respective interests and only in select cases)? Or should the agency be called upon to intervene in the litigation and thereby provide this information to the court along with its interpretive views?

Indeed, several courts have arrived at a standstill, remarking upon the absence of a full regulatory record in making what is, in essence, a fact-bound inquiry regarding the precise decisions made by the FDA at particular junctures in time. In opioid litigation, some of the courts have taken the position that the determination about whether the FDA condoned the manufacturers' actions is a factual inquiry that should not be made at the motion to dismiss stage. For example, the New Jersey state court observed that "[t]he State alleges that Purdue's marketing was inconsistent with or not covered by FDA approvals."[86] And the court reasoned, "At this stage of the litigation, the Court must accept the allegations as true and give the State all reasonable inferences."[87] The court continued, "If the State is successful on the merits, Purdue would not be forced to violate federal law. Thus, it would be possible for Purdue to comply with both New Jersey and federal laws."[88] The court thus rejected Purdue's preemption argument on the ground that no incompatibility between state and federal law had been shown;[89] indeed, given the fact-bound nature of the question, the absence of the regulatory record and any input from the FDA made this conclusion a virtual certainty.

A New Hampshire state court similarly expressed reservations about whether "it is proper to take up such a necessarily fact intensive inquiry in a motion to dismiss"[90] and refused "at this stage to

85. *Id.*

86. Grewal v. Purdue Pharma L.P., No. ESX-C-245-17, 2018 WL 4829660, at *16 (N.J. Super. Ct. Ch. Div. Oct. 02, 2018).

87. *Id.*

88. *Id.*

89. *Id.*

90. State v. Purdue Pharma Inc., No. 217-2017-CV-00402, 2018 WL 4566129, at *3 (N.H. Super. Ct. Sept. 18, 2018).

comprehensively parse each of the remaining allegations in writing."[91] Nevertheless, "[h]aving . . . reviewed the complaint and its many allegations and considered the parties' voluminous filings relevant to Purdue's motion and their accompanying exhibits, the Court conclude[d] Purdue has not shown that the State's allegations wholly reflect conduct consistent with FDA approved labeling."[92]

Faced with the absence of a sufficient regulatory record—or perhaps more likely, warring versions of the import of incomplete pieces of what is in the regulatory record—courts should consider soliciting the views of the agency. At various times in recent history, the FDA took a fairly aggressive stance toward intervening in private drug litigation, especially in cases before federal courts.[93] Moreover, even where the FDA does not intervene on its own, courts can solicit its views. Here, the practice of state and federal courts diverges. State court judges tend to be less deferential towards federal agencies. Not only are "federal courts more likely to defer to federal agencies, but—equally important in terms of explaining the decision-making process of courts—federal courts are more likely than state courts to solicit the views of the FDA."[94] Either way, once courts have summoned this key information before them, they have a significant role to play in terms of judicial oversight.

3. Judicial "Hard Look" Review

Finally, questions remain regarding the stringency of judicial review of the input from the agency. Two high profile cases provide a backdrop against which we can evaluate how the agency reference model might play out.

First, in *Shuker v. Smith & Nephew*,[95] a plaintiff was injured by a "hybrid" device. A "hybrid" device is a combination of a Class III device—which requires a full "premarket approval" ("PMA") safety review by the FDA—and Class I and II devices—which do not require full safety review and are approved through a more lenient "§ 510(k)" approval.[96] The court further described this as an

91. *Id.* at *4.

92. *Id.*

93. *See* Catherine M. Sharkey, *Federalism in Action: FDA Regulatory Preemption in Pharmaceutical Cases in State Versus Federal Courts*, 15 J. L. & POL'Y 1013, 1020 (2007).

94. *Id*. at 1020; *see also id* at 1037 ("On the whole, the FDA is far more active in the federal courts than in the state courts.").

95. Shuker v. Smith & Nephew, PLC, 885 F.3d 760 (3d Cir. 2018).

96. *Id.* at 768. According to the court, one of the device components, the "R3 metal liner" was part of the "Birmingham hip resurfacing system [BHR]," which

off-label use of the PMA component.[97] Lower federal courts are divided on the issue whether preemption analysis should apply to the "hybrid" device as a whole, or instead, to each of the separate components. With respect to the specific matter at hand, there is a strong safety-based reason to consider preemption as applied to the "hybrid" device as a whole. This is especially true given that such a device was not subjected to the FDA's rigorous PMA process to certify its safety and effectiveness. This case is unlike the situations faced by the U.S. Supreme Court in *Medtronic, Inc. v. Lohr*[98] and *Riegel v. Medtronic, Inc.*,[99] where the Court's textual analysis pointed to the significance of the stringency (or lack thereof) in the FDA's market clearing or regulatory approval process. With respect to hybrid devices, by contrast, a strict textual analysis points in one direction (preemption), whereas consideration of the FDA's lack of PMA for the device in its entirety points in the opposite direction (against preemption).

Given the novelty of applying preemption in the context of such hybrid devices, the Third Circuit Court of Appeals in *Shuker* invited the FDA to file an amicus brief addressing "whether and how § 360k(a) applies to state tort claims that concern a component of a device that received premarket approval when used in combination with components that did not."[100] The FDA endorsed the position that hybrid devices should be considered component by component. The FDA relied on the fact that the Medical Device Amendments of 1976 define "device" as follows: Any "instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, *including any component*, part, or accessory, which," among other things, is "intended to affect the structure or any function of the body."[101] The FDA reasoned that, because the definition of "device" includes component parts, it follows that any component of a PMA device also enjoys

had been granted PMA by the FDA. *Id.* The remaining components were Class II devices approved through the lenient § 510(k) process. *Id.*

97. *Id.* at 772. The R3 metal liner was approved by the FDA only for use with the PMA BHR system, and not as part of the § 510(k)-cleared R3 acetabular system. The FDA-approved label for the BHR makes this clear: "[T]he R3 metal liner is intended for use as part of the BHR system only." Amicus Letter of Food & Drug Admin. at 4, Shucker v. Smith & Nephew, Inc., 885 F.3d 760 (3d Cir. Sept. 14, 2017) (No. 16-3785) [hereinafter FDA Amicus Letter].

98. Medtronic, Inc. v. Lohr, 518 U.S. 470 (1996).

99. Riegel v. Medtronic, Inc., 552 U.S. 312 (2008).

100. FDA Amicus Letter, *supra* note 97, at 5–6.

101. *Id.* at 7 (citing 21 USC § 321(h)) (emphasis added).

§ 360k(a) preemption. The court subsequently extensively relied upon the FDA's Amicus Letter Brief throughout its decision.[102]

Second, in the recent Roundup litigation, Monsanto argued before a California federal district court that the plaintiffs' warning and design claims were impliedly preempted under Federal Insecticide, Fungicide, and Rodenticide Act ("FIFRA") because Monsanto cannot change Roundup's label or design without first obtaining approval from the Environmental Protection Agency ("EPA").[103] In this way, the EPA's review may be analogous to the FDA's safety review sufficient to establish safety standards that preempt. Further, the EPA is now proactively asserting glyphosate is not a carcinogen,[104] presumably making any state law claim requiring a carcinogenicity warning inconsistent with FIFRA requirements.

In its amicus brief on appeal at the Ninth Circuit Court of Appeals, the EPA conceded that, at the time California enacted more stringent warnings for glyphosate, the agency approved several pesticide manufacturers' applications to allow the addition of a cancer warning to the pesticide labels.[105] The EPA's current position is

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102. Though the court noted that courts "'do not defer to an agency's view' concerning preemption . . . such views as presented in amicus curiae are 'entitled to respect' . . . to the extent [they] ha[ve] the 'power to persuade.'" *Shuker*, 885 F.3d at 773 n.11 (quoting Sikkelee v. Precision Airmotive Corp., 822 F.3d 680, 693–94 (3d Cir. 2016)). The court also cited *Skidmore v. Swift & Co.*, the seminal case in which the Supreme Court laid out "this deferential approach to "the rulings, interpretations and opinions" of the administrative agency overseeing a statute. 323 U.S. 134, 140 (1944) ("While not controlling upon the courts by reason of their authority, [the rulings, interpretations and opinions of the administrator] do constitute a body of experience and informed judgment . . . [with] power to persuade, if lacking power to control.").

103. *In re* Roundup Products Liability Litigation, 364 F. Supp. 3d 1085, 1087–88 (N.D. Cal. Mar. 7, 2019) (citing *inter alia*, Wyeth v. Levine, 555 U.S. 555 (2009) (order denying motion for summary judgment)). In *Bates v. Dow Agrosciences LLC*, 544 U.S. 431 (2005), the U.S. Supreme Court outlined the scope of FIFRA's express preemption provision with respect to state failure-to-warn claims and also held that FIFRA did not preempt state claims for defective design and breach of warranty. FIFRA's express preemption of state labeling requirements is somewhat limited: So long as the warning label would still be "consistent" with the law's requirements, the label would not be preempted. *Id.* at 447.

104. Tom Polansek, *U.S. Environment Agency Says Glyphosate Weed Killer Is Not a Carcinogen*, REUTERS (Apr. 30, 2019), https://reut.rs/2xoT7Tr [https://perma.cc/93G6-WMBF].

105. *See* Brief of the United States as Amicus Curiae in Support of Monsanto at 10, Monsanto Co. v. Hardeman, No. 19-16636 (9th Cir. Dec. 20, 2019). The EPA elaborates:

> Because this listing triggered Proposition 65's warning requirements, many manufacturers that had been registered to use glyphosate reached out to EPA for guidance. Some specifically sought EPA's approval to amend their product labels to satisfy Proposition 65. EPA did approve a

that "[t]hese label-change approvals . . . were erroneous because the proposed edits warned of a cancer risk that, according to EPA's assessment, does not exist."[106] To support its significant change in position, the EPA relies on an informal communication, namely a letter to glyphosate registrants written during pendency of the litigation.[107]

As a preliminary matter, input from the EPA is relevant to the court's preemption decision. Moreover, it was the EPA's amicus brief that supplied the otherwise missing administrative record—namely reams of citations to the EPA's approval process for the pesticide, as well as its prior approval of additions to the labeling. But, in terms of the EPA's brief and the agency's arguments for preemption, the situation seems remarkably similar to *Wyeth v. Levine*; there, the U.S. Supreme Court held the plaintiff's failure-to-warn claim was not preempted even though the FDA had approved the drug's warning label, because the manufacturer could have sought a change in the label. In this case, the EPA *did* approve several label changes to warn of glyphosate's carcinogenicity after California added the chemical as a possible carcinogen subject to the labeling requirements of Proposition 65. Monsanto, therefore, had an uphill battle to argue that it could not have warned of those risks when the agency has a history of approving pesticide label changes for this specific chemical and cancer risk. It is significant that the EPA has acknowledged its prior record on the chemical and indeed supplied the information as part of the administrative record before the court.

The EPA, moreover, is currently undertaking a revision to registration requirements for glyphosate, a process that allows for public comment and assessment of whether the labeling requirements are consistent with FIFRA's mandate to protect public health and the environment.[108]

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limited number of applications allowing the addition of a Proposition 65 glyphosate cancer warning to pesticide labels when requested.

Id.

106. *Id.* at 10.

107. *Id.* at 11 ("In an August 7, 2019 letter, EPA informed all glyphosate registrants that EPA had concluded glyphosate is 'not likely to be carcinogenic to humans.'"). According to the EPA, it "then stated that products bearing a Proposition 65 warning statement due to the presence of glyphosate are misbranded under FIFRA because such a statement is 'false and misleading.'" *Id.* Perhaps in an effort to provide a pivotal point that predates the litigation, the EPA explains that in a 2019 letter citing to a scientific review from 2017, the agency concluded that glyphosate was not carcinogenic. *Id.*

108. Glyphosate Proposed Interim Registration Review Decision; Notice of Availability, 84 Fed. Reg. 19,782 (May 6, 2019). NRDC filed comments laying out

Under the agency reference model, applying heightened scrutiny to the agency's views on implied preemption, the court should give little weight to the EPA's views for two reasons. First, the agency has changed its position without providing sufficient empirical evidence to support a reasoned basis for its newly adopted view. And even more significantly, there is an ongoing process for the EPA revisions to the registrations requirements for glyphosate. The preemption context provides an avenue for a kind of indirect challenge to the agency's registration decision; but because the direct administrative law process is underway, it would make sense for the court to hold off, pending the conclusion of the administrative process, perhaps via the doctrine of primary jurisdiction.[109]

CONCLUSION: ACCOUNTABILITY LOOPHOLE

The FDA has, thus far, been largely missing in action throughout the opioid litigation. Yet, at the same time, it has played a major role in pre-market review and post-market surveillance of prescription opioids. Even those who are hostile to federal preemption defenses and/or champion any move that makes it more likely drug manufacturers will be held liable for state tort actions should be concerned by this state of affairs. When courts summarily dismiss (or ignore altogether) the manufacturers' preemption arguments, they forfeit an opportunity to hold the FDA accountable. If, instead, courts applied the agency reference model to (1) require the agency to set forth and justify its regulatory actions and (2) subject the input received from the agency to heightened judicial review, the FDA could no longer sit silent on the sidelines. The FDA is off the hook for the time being as it remains in the periphery of the raging debate regarding responsibility for the opioid cri-

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the disagreements within the agency about whether the December 2017 assessment was done correctly. *See* NAT. RES. DEF. COUNCIL, *Comments from the Natural Resources Defense Council: Glyphosate Proposed Interim Registration Review Decision*, 3–4 (Sept. 3, 2019), https://bit.ly/3an6WQW [https://perma.cc/G8CZ-M3E2]. I am grateful to Rachel Rothschild (NYU Law 2020) for bringing this to my attention.

109. For elaboration of primary jurisdiction, see Catherine M. Sharkey, *Tort-Agency Partnerships in an Age of Preemption*, 15 THEORETICAL INQUIRIES IN LAW 359, 383–84 (2014).

> Under the doctrine of primary jurisdiction, a court may "refer a matter extending beyond the 'conventional experiences of judges' or 'falling within the realm of administrative discretion' to an administrative agency with more specialized experience, expertise, and insight.'" . . . . The effect is that "the judicial process is suspended pending referral of such issues to the administrative body for its views."

Id. (quoting Nat'l Commc'ns Ass'n Inc. v. AT&T Co., 46 F.3d 220, 222–23 (2d Cir. 1995).

sis. To date, only bits and pieces of the FDA's prescription opioid regulatory history has been considered by the courts. The time has come for courts to close the accountability loophole and call upon the FDA to speak.